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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/004,968	12/05/2001	Davis T.W. Ng	P05424US1	7842

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EXAMINER

VOGEL, NANCY S

ART UNIT	PAPER NUMBER
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1636

DATE MAILED: 01/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No. 10/004,968	Applicant(s) NG ET AL.	
	Examiner Nancy Vogel	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 19 December 2003.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-42 is/are pending in the application.
- 4a) Of the above claim(s) 13,14,24,25 and 32-42 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-12,15-23 and 26-31 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 05 December 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All   b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                      | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                             | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>1 and 2</u> | 6) <input type="checkbox"/> Other: _____                                    |

## **DETAILED ACTION**

### ***Election/Restrictions***

Applicant's election with traverse of Group I, claims 1-12, 15-23, 26-31 in the paper filed 12/19/03 is acknowledged. The traversal is on the ground(s) that the search for the groups is the same since they all concern heterologous proteins in fungi. This is not found persuasive because it is maintained that due to the separate subject matter of each group (i.e. proteins, fungal organisms, genetic method) the searches for each group would not be the same. While the groups may be connected by an inventive concept, the subject matter remains distinct.

The requirement is still deemed proper and is therefore made FINAL.

Claims 13, 14, 24, 25, 32-42 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the paper filed 12/19/03.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-9, and 15-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Tanner et al. (US Pat. No. 5,714,377) (cited on Information Disclosure Statement submitted by applicant on 7/7/03).

Tanner et al. disclose a method of producing a heterologous protein in a fungi, which is a yeast cell, comprising providing a yeast cell having a mutation in a genePMT1 gene, in which O-glycosylation is inhibited (see col. 2 line 52- col. 6, line 62). The transformation method may be the LiAc method or any other technique disclosed in the literature (see col. 5, lines 48-59). A yeast based plasmid may be used (see col. 5, lines 30-47).

Claims 1, 2, 5, 6, 7, 15, 16, 19, 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Ernst et al. (WO 94/26873) (cited on Information Disclosure Statement submitted by applicant on 7/7/03).

Ernst et al. disclose a method of producing a heterologous protein in fungi comprising providing a recipient cell in which O-glycosylation is inhibited, and introducing a polynucleotide expression construct (see page 3, lines 14-19 and line 33 – page 4, line 23 and page 9, lines 5-20, and claims). The polynucleotide may be within a yeast based plasmid (see page 9 lines 11-14). The recipient cell has inhibited o-

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glycosylation activity, and the defect is in a protein mannosyltransferase (see page 1, lines 5-11, page 3, lines 33-page 4, line 22).

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-7, and 15-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ernst et al. (WO 94/26873) (cited on Information Disclosure Statement submitted by applicant on 7/7/03) in view of Ito et al. (J. Bacteriol., 153 (1): 163-8 (1983)).

Ernst et al. is cited essentially for the reasons set forth above. The difference between the reference and the instant claims is that the use of LiAc transformation is not disclosed.

However, Ito et al. disclose a method for transformation of yeast using LiAc, and further disclose that the method is advantageous since it is simple, easy time saving, results in transformation efficiency comparable with the protoplast method, has the advantage of being able to replica plat colonies since no regeneration agar is necessary, and applicability to yeast cells that are resistant or sensitive to lytic enzymes (see paragraph bridging columns 1 and 2, page 168). It would have been obvious to one of ordinary skill in the art to use the well known LiAc transformation method disclosed by Ito et al. in the method of producing a heterologous protein, as disclosed by Ernst et al. because Ernst et al. teach that it is within the ordinary skill in the art to introduce an expression construct into fungi to produce a heterologous protein and Ito et al. teach that it is within the ordinary skill in the art to transform yeast using LiAc. One would have been motivated to utilize this method by its well known advantages of speed, high frequency of transformation, and ease of use, as disclosed by Ito et al. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claims 1-10, 15-23, are rejected under 35 U.S.C. 103(a) as being unpatentable over Tanner et al. (US Pat. No. 5,714,377) in view of Strahl-Bolsinger et al. (Biochim. Biophys. Acta 1426: 297-307 (1999), cited by applicant).

Tanner et al. disclose a method of producing a heterologous protein in a fungi, which is a yeast cell, comprising providing a yeast cell having a mutation in a genePMT1 gene, in which O-glycosylation is inhibited (see col. 2 line 52- col. 6, line 62). The transformation method may be the LiAc method or any other technique disclosed in the literature (see col. 5, lines 48-59). A yeast based plasmid may be used (see col. 5, lines 30-47). Tanner et al. disclose that it is advantageous to inhibit O-glycosylation when producing heterologous proteins in yeast since such glycosylation patterns are not present on the native non-yeast proteins, and may result in altered pharmacokinetic properties and biological properties.

The difference between Tanner et al. and the claimed invention is that the PMT gene is PMT 2 (claims 10 and 23), or any of PMT 1-6 (claim 21).

However, Strahl-Bolsinger et al. disclose that the protein encoded by PMT2 shares homology and similar function in O-mannosylation activity to PMT1 (see page 298, second column) and therefore is functionally equivalent to PMT1. In addition, the reference discloses that the PMT1-6 genes all share homology and activity as protein O-mannosyltransferases (see bottom of page 298), indicating that defects in any of the PMT 1-6 genes results in inhibition of O-glycosylation.

It would have been obvious to one of ordinary skill in the art to substitute for the yeast cell having a mutation in the PMT 1 gene in the method taught by Tanner et al.,

with a yeast cell having a mutation in any one of the PMT2-6 genes as taught by Strahl-Bolsinger et al. because Tanner et al. teach that it is within the ordinary skill in the art to produce heterologous protein in yeast cells in which O-glycosylation is inhibited and Strahl-Bolsinger et al. teach that O-glycosylation can be inhibited by defects in any other PMT 1-6 genes. One would have motivated to do for the expected benefit of using yeast cells having different defects in O-glycosylation in the method taught by Tanner et al. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection is based on the Guidelines for the Examination of Patent Applications under the 35 U.S.C. 112, first paragraph "Written Description published in the Federal Register (Volume 66, Number 4, Pages 1099-1111). The claims are drawn



to a method of producing heterologous proteins in fungi comprising providing a recipient fungi cell wherein the quality control mechanism in said cell is modified so that incompletely folded heterologous proteins are not degraded in the endoplasmic reticulum. The specification defines the quality control mechanism as that mechanism by which yeast return misfolded proteins to the cytosol for degradation (page 4 of the specification). Claims 1-5 are genus claims in terms of a method using any recipient fungi cell wherein the cell has any modification in which incompletely folded heterologous proteins are not degraded in the endoplasmic reticulum. The disclosure is not deemed to be descriptive of the complete structure of a representative number of species encompassed by the claims as one of skill in the art cannot envision all the methods using modified recipient fungi cells based on the teachings of the specification. While the specification provides general information regarding the use of yeast PMT (protein mannosyltransferase) and BST (Bypass of sec 13) mutants for the production of heterologous proteins, there is no disclosure of common structure possessed by fungi cells which would result in the lack of degradation of incompletely folded heterologous proteins. There is no structure/function analysis of the disclosed yeast PMT or BST mutant cells to provide guidance on the essential genes that could be inhibited and result in the claimed characteristics. Therefore, the specification does not describe the claimed method for producing a heterologous protein in fungi, utilizing as a recipient cell a fungi wherein the quality control mechanism is modified so that incompletely folded heterologous proteins are not degraded in the endoplasmic reticulum in such full, clear, concise and exact terms so as to indicate that Applicant had

possession of the method at the time of filing the present application. Thus, the written description requirement has not been satisfied.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7-12, 15-23 and 26-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 7, and by dependence claims 7-12, are vague and indefinite in the recitation of "said recipient cell comprises inhibition of a protein mannosyltransferase gene". It is not clear what is intended by this phrase. Is it intended to mean that the expression of a gene encoding protein mannosyltransferase is inhibited, or that the activity of the product of the protein mannosyltransferase gene is inhibited, or something else? In the interest of compact prosecution, the claim has been examined as if it recited: "The method of claim 6 wherein said recipient cell is modified so that the expression of a protein mannosyltransferase gene is inhibited".

Claim 11 recites the limitation "said recipient gene" in line 1. There is insufficient antecedent basis for this limitation in the claim. It is noted that if one of the PMT 1-6 genes recited in claim 8 are intended as the "recipient gene", it is not understood how it "provides inhibition" of the Bypass of Sec Thirteen gene, since they encode protein mannosyltransferase, rather than a regulatory protein. Clarification is required.

Claim 26, and by dependence, claims 27-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 15 and 26, and by dependence claims 16-23, and 27-31 are vague and indefinite in its recitation of "structural gene". It is not known what is intended by this phrase.

**Conclusion**

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy Vogel whose telephone number is (571) 272-0780. The examiner can normally be reached on Monday through Friday, 6:30AM – 3:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is (703) 305-3014.

ntv

  
TERRY MCKELVEY  
PRIMARY EXAMINER